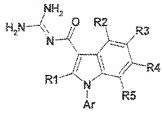
This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims

1. (Original) A compound of the formula (I)



(I)

wherein,

R1 is hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,

R2 is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, NRaRb or polyfluoroalkyl having 1, 2, 3 or 4 carbon atoms,

Ra and Rb

are independently of each other hydrogen, linear or branched alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or Ra and Rb form, together with the nitrogen atom to which they are attached, a 5- or 6-membered heterocycle, which may optionally contain another hetero atom chosen from O, S and N,

R3 is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms or hydroxyl,

R4 is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms or hydroxyl,

R5 is hydrogen or halogen,

Ar is a 9- or a 10-membered bicyclic heteroaryl having one, two or three nitrogen atoms, which may be linked via any of its positions,

or a racemic mixture, enantiomer, diastereomer, or tautomer of such compound, or a mixture thereof, or a pharmaceutically acceptable salt of such compound, racemic mixture, enantiomer, diastereomer, tautomer, or mixture.

2. (Original) A compound according to claim 1, wherein

R1 is hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,

R2 is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, NRaRb or polyfluoroalkyl having 1, 2, 3 or 4 carbon atoms,

Ra and Rb

are independently of each other hydrogen, linear or branched alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or Ra and Rb form, together with the nitrogen atom to which they are attached, a 5- or 6-membered heterocycle, which may optionally contain another hetero atom chosen from O, S and N,

R3 is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms or hydroxyl,

R4 is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms or hydroxyl,

R5 is hydrogen or halogen,

Ar is quinoline, isoquinoline, cinnoline or 7H-pyrrolo-[2,3-d]-pyrimidine, which may be linked via any of its positions.

3. (Original) A compound according to claim 1 wherein

R1 is hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,

R2 is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, NRaRb or polyfluoroalkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,

Ra and Rb

are independently of each other hydrogen, linear or branched alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or Ra and Rb form, together with the nitrogen atom to which they are attached, a 5- or 6-membered heterocycle, which may optionally contain another hetero atom chosen from O, S and N,

R3 is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms or hydroxyl,

R4 is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms or hydroxyl,

R5 is hydrogen or halogen,

Ar is quinoline, which may be linked via any of its positions.

4. (Original) A compound according to claim 1 wherein

R1 is hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,

R2 is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, NRaRb or polyfluoroalkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,

Ra and Rb

are independently of each other hydrogen, linear or branched alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or Ra and Rb form, together with the nitrogen atom to which they are attached, a 5- or 6-membered heterocycle, which may optionally contain another hetero atom chosen from O, S and N,

R3 is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms or hydroxyl,

R4 is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms or hydroxyl,

R5 is hydrogen or halogen,

Ar is isoquinoline, which may be linked via any of its positions.

5. (Original) A compound according to claim 1 which is:

3-guanidinocarbonyl-1-(isoquinol-1-yl)-1H-indole,

3-guanidinocarbonyl-1-(quinol-4-yl)-1H-indole,

3-guanidinocarbonyl-1-(quinol-2-yl)-1H-indole,

3-guanidinocarbonyl-1-(isoquinol-1-yl)-5-methyl-1H-indole,

3-guanidinocarbonyl-5-methyl-1-(quinol-2-yl)-1H-indole,

3-guanidinocarbonyl-5-methyl-1-(quinol-4-yl)-1H-indole,

3-guanidinocarbonyl-1-(quinol-3-yl)-1H-indole,

3-guanidinocarbonyl-1-(quinol-6-yl)-1H-indole,

3-guanidinocarbonyl-1-(quinol-8-yl)-1H-indole,

3-guanidinocarbonyl-1-(isoquinol-3-yl)-1H-indole,

3-guanidinocarbonyl-6-methoxy-1-(quinol-4-yl)-1H-indole,

3-guanidinocarbonyl-6-hydroxy-1-(quinol-4-yl)-1H-indole,

6-fluoro-3-guanidinocarbonyl-1-(quinol-4-yl)-1H-indole,

5-fluoro-3-guanidinocarbonyl-1-(quinol-4-yl)-1H-indole,

4-chloro-3-guanidinocarbonyl-1-(quinol-4-yl)-1H-indole,

5-chloro-3-guanidinocarbonyl-1-(quinol-4-yl)-1H-indole,

6-chloro-3-guanidinocarbonyl-1-(quinol-4-yl)-1H-indole,
4-fluoro-3-guanidinocarbonyl-1-(quinol-4-yl)-1H-indole,
3-guanidinocarbonyl-4-methyl-1-(quinol-4-yl)-1H-indole,
3-guanidinocarbonyl-4-trifluoromethyl-1-(quinol-4-yl)-1H-indole,
4-dimethylamino-3-guanidinocarbonyl-1-(quinol-4-yl)-1H-indole,
3-guanidinocarbonyl-1-(cinnolin-4-yl)-1H-indole, or
5-methoxy-3-guanidinocarbonyl-1-(cinnolin-4-yl)-1H-indole,
or a tautomer thereof or a pharmaceutically acceptable salt of such compound or tautomer.

6. (Original) A pharmaceutical composition for human, veterinary, or phytoprotective use comprising an effective amount of a compound according to claim 1 together with a pharmaceutically acceptable medium.

7. (Canceled).

8. (Previously presented) A method for the treatment of cardiovascular disease, metabolic disease, cancerous disease, or fibrotic disease comprising administering to a patient in need thereof, an effective amount of a compound according to claim 1 to inhibit the cellular sodium-proton antiporter (Na+/H+-exchanger) activity of said patient.

9. (Previously presented) A method for the treatment of

acute or chronic damage to, or disorders or indirect sequelae of organs and tissues caused by ischemic or reperfusion events;

arrhythmias, life-threatening cardiac ventricular fibrillation, myocardial infarction, angina pectoris;

ischemic states of the heart, ischemic states of the peripheral and central nervous system, stroke, cerebral oedema attack, ischemic states of peripheral organs and tissues;

states of shock;

diseases in which cellular proliferation represents a primary or secondary cause;

cancer, metastasis, prostate hypertrophy, prostate hyperplasia;

atherosclerosis, disturbances of lipid metabolism, high blood pressure;

disorders of the central nervous system;

non-insulin-dependent diabetes mellitus, late damage from diabetes;

thromboses, disorders resulting from endothelial dysfunction, intermittent claudication;

fibrotic disorders of internal organs, fibrotic disorders of the liver, fibrotic disorders of the kidney, fibrotic disorders of vessels, fibrotic disorders of lung, fibrotic disorders of the heart;

heart failure, congestive heart failure, acute or chronic inflammatory disorders, disorders caused by protozoa;

malaria, or coccidiosis in poultry, comprising administering to a patient in need thereof, an effective amount of a compound according to claim 1 to inhibit the cellular sodium-proton antiporter (Na+/H+-exchanger) activity of said patient.

10. (Previously presented) A method according to claim 9 for the treatment of allergic shock, cardiogenic shock, hypovolaemic shock or bacterial shock.

11. (Previously presented) A method according to claim 9 for the treatment of essential hypertension.

12. (Previously presented) A method according to claim 9 for the treatment of disorders resulting from overexcitability of the CNS.

13. (Previously presented) A method according to claim 12, for the treatment of epilepsy or centrally induced convulsions.

14. (Previously presented) A method according to claim 9 for the treatment of anxiety states, depressions or psychoses.

15. (Previously Presented) A method for protecting an organ in a transplant donor during organ transplantation, both before and during the removal of the organ, comprising administering to said donor, an effective amount of a compound according to claim 1 to inhibit the cellular sodium-proton antiporter (Na+/H+-exchanger) activity of said donor.

16. (Previously Presented) A method for protecting a removed organ during treatment with, or storage in physiological bath liquids, comprising contacting said organ with a compound

according to claim 1 to inhibit the cellular sodium-proton antiporter (Na+/H+-exchanger) activity of said organ.

17. (Previously Presented) A method for protecting a removed organ during transfer to a recipient organism during organ transplantation, comprising contacting said organ with a compound according to claim 1 to inhibit the cellular sodium-proton antiporter (Na+/H+-exchanger) activity of said organ.

18. (Previously Presented) A method for preventing age-related tissue change, in a patient in need thereof, comprising administering to said patient, an effective amount of a compound according to claim 1 to inhibit the cellular sodium-proton antiporter (Na+/H+-exchanger) activity of said patient.

19. (Previously Presented) A method for prolonging life in a patient in need thereof, comprising administering to said patient, an effective amount of a compound according to claim 1 to inhibit the cellular sodium-proton antiporter (Na+/H+-exchanger) activity of said patient.

20. (Previously Presented) A method for the treatment or reduction of the cardiotoxic effects in thyrotoxicosis in a patient in need thereof, comprising administering to said patient an effective amount of a compound according to claim 1 to inhibit the cellular sodium-proton antiporter (Na+/H+-exchanger) activity of said patient.

21 - 35. (Canceled).

36. (Previously presented) A method for the treatment of acute or chronic damage, disorders or indirect sequelae of organs or tissues caused by ischemic or reperfusion events in a patient in need thereof, comprising administering to said patient an effective amount of a compound according to claim 1 to inhibit the cellular sodium-proton antiporter (Na+/H+-exchanger) activity of said patient.

37. (Canceled).

38. (Previously presented) A method for the treatment of life-threatening cardiac ventricular fibrillation, in a patient in need thereof, comprising administering to said patient, an effective amount of a compound according to claim 1 to inhibit the cellular sodium-proton antiporter (Na+/H+-exchanger) activity of said patient.

39. (Canceled).

40. (Previously presented) A method for the treatment of metastasis in a patient in need thereof, comprising administering to said patient an effective amount of a compound according to claim 1 to inhibit the cellular sodium-proton antiporter (Na+/H+-exchanger) activity of said patient.

41. (Canceled)

42. (Previously presented) A method for the treatment of fibrotic disorders of the heart, heart failure, or congestive heart failure, in a patient in need thereof, comprising administering to said patient an effective amount of a compound according to claim 1 to inhibit the cellular sodium-proton antiporter (Na+/H+-exchanger) activity of said patient.

43. (Canceled)

44. (Previously presented) A method for the treatment of a disease which is related to NHE, in a patient in need thereof, comprising administering to said patient an effective amount of a compound according to claim 1 to inhibit the cellular sodium-proton antiporter (Na+/H+-exchanger) activity of said patient.

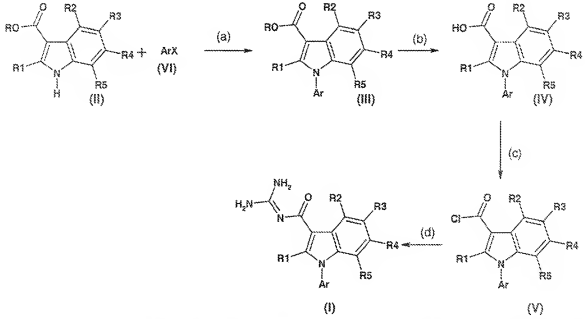
45. (Canceled)

46. (Previously presented) A method for the treatment of a disease which is related to NHE1, in a patient in need thereof, comprising administering to said patient an effective amount of a compound according to claim 1 to inhibit the cellular sodium-proton antiporter (Na+/H+-exchanger) activity of said patient.

47. (Canceled)

48. (Previously Presented) A method for protecting the organs or blood vessels during surgical intervention, in a patient in need thereof, comprising administering to such patient an effective amount of a compound according to claim 1 to inhibit the cellular sodium-proton antiporter (Na+/H+-exchanger) activity of said patient.

49. (Original) A process for the preparation of a compound according to claim 1 characterised in that



a) a heteroaryl halide ArX of the formula (VI) is reacted with a 3-alkoxycarbonyl-1H-indole of the formula (II)

b) the obtained 3-alkoxycarbonyl-1-heteroaryl-indole of the formula (III) is saponified

c) the 3-carboxy-1-heteroaryl-indole of the formula (IV) is converted in the acid chloride of formula (V)

d) the obtained product of formula (V) is reacted with guanidine,

the product is isolated and is optionally converted into a pharmaceutically acceptable salt,

wherein in the compounds of the formula II, III, IV, V and VI

Ar, R1, R2, R3, R4 and R5 are defined as in claim 1,

X is F, Cl, Br or I and

R is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms.

50. (Previously presented) A method for the treatment of cardiovascular disease, metabolic disease, cancerous disease, or fibrotic disease comprising administering to a patient in need thereof, an effective amount of a compound according to claim 1.

51. (Previously presented) A method for the treatment of

acute or chronic damage to, or disorders or indirect sequelae of organs and tissues caused by ischemic or reperfusion events;

arrhythmias, life-threatening cardiac ventricular fibrillation, myocardial infarction, angina pectoris;

ischemic states of the heart, ischemic states of the peripheral and central nervous system, stroke, cerebral oedema attack, ischemic states of peripheral organs and tissues;

states of shock;

diseases in which cellular proliferation represents a primary or secondary cause;

cancer, metastasis, prostate hypertrophy, prostate hyperplasia;

atherosclerosis, disturbances of lipid metabolism, high blood pressure;

disorders of the central nervous system;

non-insulin-dependent diabetes mellitus, late damage from diabetes;

thromboses, disorders resulting from endothelial dysfunction, intermittent claudication;

fibrotic disorders of internal organs, fibrotic disorders of the liver, fibrotic disorders of the kidney, fibrotic disorders of vessels, fibrotic disorders of lung, fibrotic disorders of the heart;

heart failure, congestive heart failure, acute or chronic inflammatory disorders, disorders caused by protozoa;

malaria, or coccidiosis in poultry, comprising administering to a patient in need thereof, an effective amount of a compound according to claim 1.

52. (Original) A method for protecting an organ in a transplant donor during organ transplantation, both before and during the removal of the organ, comprising administering to said donor, an effective amount of a compound according to claim 1.

53. (Original) A method for protecting a removed organ during treatment with, or storage in physiological bath liquids, comprising contacting said organ with a compound according to claim 1.

54. (Original) A method for protecting a removed organ during transfer to a recipient organism during organ transplantation, comprising contacting said organ with a compound according to claim 1.

55. (Original) A method for preventing age-related tissue change, in a patient in need thereof, comprising administering to said patient, an effective amount of a compound according to claim 1.

56. (Original) A method for prolonging life in a patient in need thereof, comprising administering to said patient, an effective amount of a compound according to claim 1.

57. (Original) A method for the treatment or reduction of the cardiotoxic effects in thyrotoxicosis in a patient in need thereof, comprising administering to said patient an effective amount of a compound according to claim 1.

58. (Previously presented) A method for the treatment of acute or chronic damage, disorders or indirect sequelae of organs or tissues caused by ischemic or reperfusion events in a patient in need thereof, comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1.

59. (Original) A method for the treatment of life-threatening cardiac ventricular fibrillation, in a patient in need thereof, comprising administering to said patient, a pharmaceutically effective amount of a compound according to claim 1.

60. (Previously presented) A method for the treatment of metastasis in a patient in need thereof, comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1.

61. (Previosly presented) A method for the treatment of fibrotic disorders of the heart, heart failure, or congestive heart failure, in a patient in need thereof, comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1.

62. (Previously presented) A method for the treatment of a disease which is related to NHE, in a patient in need thereof, comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1.

63. (Previsously presented) A method for the treatment of a disease which is related to NHE1, in a patient in need thereof, comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1.

64. (Original) A method for protecting the organs or blood vessels during surgical intervention, in a patient in need thereof, comprising administering to such patient a pharmaceutically effective amount of a compound according to claim 1.